Effects of a Foregoing Fast on Plasma Insulin Patterns in Unanaesthetized Rats during Intravenous Glucose Infusions and during Food Intake

Strubbe, J.H.

Published in:
Diabetologia

Although less lactate was produced by insulin deficient muscle during exercise ($p < 0.05$), the differences in venous blood-pH appeared to be caused mainly by different CO_2-production by the exercising muscle in the two groups. Data of ketone body metabolism suggested that there might have been an inadequate response of Krebs-cycle activity to exercise in insulin-deficient muscle. This study indicates that altered calf muscle metabolism in insulin deficiency can impair locally the oxygen delivery capacity of blood.

248. The Effect of Insulin and Glucose on Sterol Synthesis in Cultured Arterial Smooth Muscle Cells.

R. W. Stout. Department of Medicine, The Queen's University of Belfast, N. Ireland.

Recent evidence suggests that the smooth muscle cell plays a key role in the process of atherogenesis, proliferating in the arterial intima in the early stages of the disease and becoming filled with lipid as the disease processes. Previous experiments have shown that insulin stimulates the proliferation of cultured primate arterial smooth muscle cells. In these experiments the effect of insulin and glucose on sterol synthesis was studied. Arterial smooth muscle cells were cultured from pieces of intima and inner media of young rat aortas. The cells were grown in petri dishes in culture medium with foetal calf serum and when confluent were exposed to insulin or glucose for 24 hours. Insulin in concentrations of 1–100 mU per ml stimulated the incorporation of sodium acetate-2-^{14}C into non-saponifiable lipids and digitonin precipitable sterols. However, insulin had no effect on the incorporation of labelled mevalonate into cell sterols. Increasing concentrations of glucose in the medium up to 140 mM had no effect on the incorporation of isotope into sterols, but higher concentrations of glucose caused cell damage and sterol synthesis was markedly depressed. These results may have relevance to the development of atherosclerosis in diabetes and obesity.

249. Effects of a Foregoing Fast on Plasma Insulin Patterns in Unanaesthetized Rats during Intravenous Glucose Infusions and during Food Intake.

J. H. Strubbe. Zoological Laboratory, State University of Groningen, Haren (Gr.), The Netherlands.

Fasting is known to inhibit the insulinogenic effect of glucose. The aim of this study was to investigate whether the well-known two phases of the secretory responses were both affected after fasting. Male Wistar rats, provided with double heart catheters for continuous intravenous glucose infusions and blood sampling from the freely moving unanaethetized animals, received glucose infusions lasting 15 minutes in the fed state and after food deprivation for 24 hrs. In another experiment they were allowed to eat a standard meal under both conditions. Fasting reduced both phases of the response almost equally. After fasting a sluggish start of the second phase was very prominent. A short pre-infusion of glucose, given 10 minutes before a 15 minute infusion, decreased the first phase of the response to the latter only after fasting. The second phase was unaffected. These results show that fasting reduced both phases of the insulin response. A decreased first phase in the deprived condition after pre-infusion with glucose suggests a slower replenishment of the first phase "compartment" indicating slower granule transport within the B-cell after food deprivation.

250. Effect of Progesterone and Oestradiol on Insulin Secretion: Importance during Pregnancy in the Rat.

B. Ch. J. Sutter, M.-Th. Sutter-Dub and R. Jacquot. Laboratoire de Physiologie Animale, Université de Reims. Present address: Laboratoire d'Endocrinologie, Avenue des Facultés, F–33405 Talence Cedex, France.

During gestation and lactation serum IRI is higher than in non pregnant rats; glycaemia is normal. This can be explained by insulin resistance related to hormones involved in these physiological stages. But it is also possible that female sex hormones act on glucose induced insulin secretion. Rat pancreas is first perfused in situ by a 0.8 mg/ml glucose containing buffer; insulin secretion is stimulated by 1.4 mg/ml glucose during one hour. IRI, oestradiol (E_2) and progesterone (P) are measured by radioimmunoassays. Glucose induced insulin secretion from pregnant rats (10 and 20 days) is enhanced when compared to that of normal female. Insulin secretion at day 20 is higher than at day 10. – 3 weeks P (5 mg/day) or E_2 (0.1 mg/day) treatments increase IRI secretion. – P (2.5 μg/ml) added to the perfusion milieu has a smaller effect than E_2 (0.05 μg/ml) or E_2 + P on the increase of IRI release from normal female pancreas. – IRI secretion in the castrated female is only increased by E_2 or E_2 + P. In contrast to E_2, P has no direct effect on glucose induced insulin release. In combination the two hormones increase markedly the IRI secretion. The increased insulin secretion after the 3 weeks treatment by progesterone can be due to the peripheral resistance developed against insulin effect by progesterone. As serum oestradiol concentrations are low at day 10 of gestation and high at day 20 this can explain the greater IRI release at day 20 than at day 10. Finally, these two hormones play a role in the regulation of IRI secretion in the rat during pregnancy and perhaps during lactation.

251. Epidemiological Factors Relating to the High Diabetic Prevalence on a Pacific Island.

P. Taft, P. Zimmet, A. Guinea, D. Bennett, H. Ringrose and K. Thoma. Department of Metabolic Medicine and Epidemiology, Southern Memorial Hospital and Ewen Downie Metabolic Unit, Alfred Hospital, Melbourne, Australia.

A high diabetes prevalence has been demonstrated on an isolated, urbanized Central Pacific island. 34.4% of the population aged 15 years and over were diabetic (2 hour plasma glucose 160 mg/100 ml). 11.3% were borderline diabetes (2 hour plasma glucose 140 to 159 mg/100 ml) and 54.3% had normal glucose tolerance. Possible factors relating to the high prevalence were studied. From a genetic view point, 60% of those studied had a family history of diabetes. A separate dietary survey showed a mean caloric intake of 6,126 cal/day – 48% carbohydrate, 33% fat and 15% protein. There appeared to be an association between degree of adiposity and diabetes – the mean weight of normal subjects was 80.6 kg compared with 86.2 kg in diabetics. The mean body mass index (W/H^2) was 31.6 in normals and 33.9 in diabetics. There was a relationship between parity and diabetes – the mean number of full-term pregnancies being 2.9 in normal, 4.1 in borderline and 5.8 in diabetic women. Thus it appears that genetic and cultural factors as well as factors associated with urbanization may play a role in the high prevalence rate seen in this island population.

252. The B-Cell's Monovalent Cation Pump as a Potential Target for Diabetogenic Damage: Sensitivity to Alloxan and Protection by Sugars.

I.-B. Täljedal. Department of Histology, University of Umeå, S–901 87 Umeå, Sweden.

The B-cell's monovalent cation pump is probably important for insulin secretion. It transports Rb^+ vigorously, but the absence of an impressive Na^+ gradient and easily demonstrable Na^+/K^+-ATPase makes its true nature seem obscure. A new approach to characterizing the pump was discovered im experiments aimed at establishing a good model for analysing alloxan's β-cytotoxicity in vitro. ob/ob-Mouse islets were incubated with $^{86}RbCl$ and test substances in bicarbonate buffer. Preincubation with 0.5-5 mM alloxan for 10 min caused a graded inhibition of the Rb^+ accumulation. The effect had a latency of about 1 min and was due to inhibited Rb^+ entry rather than an increased Rb^+ permeability and exit rate. D-Glucose, 2-20 mM, protected against alloxan in a dose-dependent manner, and this protection was reproduced with 3-O-methyl-D-glucose but not L-glucose or mannoheptulose; mannoheptulose prevented the effect of D-glucose. Alloxan caused a marginal decrease of ATP, but not glucose-6-phosphate or the ouabain-inhibitable ATPase and aryl phosphatase activities. The results explain the membrane-depolarizing effect of alloxan and suggest that inhibition of the B-cell's monovalent cation pump may be fundamental to alloxan diabetes and represent an important parameter in the screening for natural factors with potential diabetogenic action.

253. Effects of Calcium Ionophores on Pancreatic B-Cell Metabolism.

J. Tamarit-Rodriguez. Department of Histology, University of Umeå, S–901 87 Umeå 6, Sweden.

Previous studies have indicated that exposure of pancreatic B-cells to the ionophores X-537A and A-23187 modifies insulin release